This listing of claims will replace all prior versions and listings of claims in the prior application:

Claim 1 (currently amended): A method of treating an organism for a condition which is mediated by COX-2 expression, the method comprising the step of orally, parenterally, or rectally administering to the organism a composition comprising a therapeutically or ~~prophylatically~~ prophylactically effective COX-2 inhibiting amount of an organic extract of a plant, wherein the extract selectively inhibits the activity of COX-2 relative to COX-1 as determined in vitro by an IC_{50} ratio of COX-1/COX-2, and wherein the plant is selected from the order consisting of Agavales, Apocynales, Arales, Asterales, Basidiomycetae, Brassicales, Caryophyllales, Cycadales, Ebenales, Euphorbiales, Fagales, Hydrocharitales, Lamiales, Liliales, Loasales, Malvales, Myrtales, Palmales, Pandanales, Papaverales, Piperales, Polemoniales, Polygalales, Primulales, Ranales, Rhamnales, Rosales, Rubiales, Rutales, Santalales, Sapindales, Scrophulariales, Umbellales, Urticales, and Violales.

Claim 2 (original) The method of claim 1 wherein the inhibitory effect of the extract on COX-2 activity is greater than or equal to about 2 times greater than the inhibitory effect of the extract on COX-1 activity.

Claim 3 (previously presented) The method of claim 1 wherein the inhibitory effect of the extract on COX-2 activity is greater than or equal to about 10 times greater than the inhibitory effect of the extract on COX-1 activity.

Claims 4-57 (canceled)

Claim 58 (original) The method of claim 1 wherein the extract of the Polemoniales order is selected from the families consisting of Boraginaceae and Solanaceae.

Claim 59 (canceled)

Claim 60 (original) The method of claim 58 wherein the extract of the Solanaceae family is selected from the genera consisting of Capsicum and Solanum.

Claims 61-96 (canceled)

Claim 97 (currently amended): The method of claim 1 wherein the organic extract is ~~a purified composition~~ obtained by a method comprising:

(a) contacting the plant with an organic solvent to remove an extract from the plant wherein the extract selectively inhibits COX-2 activity; and

(b) isolating the extract with COX-2 inhibitory activity.

Claim 98 (currently amended): The method of claim 97 ~~wherein the extract selectively inhibits COX-2 activity~~ wherein the inhibitory effect of the organic extract on COX-2 activity is greater than or equal to about 2 times greater than the inhibitory effect of the extract on COX-1 activity.

Claim 99 (original) The method of claim 97 wherein step (a) further comprises mixing the plant with the organic solvent and stirring the resulting mixture at a temperature between about 25°C and the boiling point of said solvent for at least one minute.

Claim 100 (original) The method of claim 97 wherein the organic solvent is selected from the group consisting of hydrocarbon solvents, ethers, chlorinated solvents, acetone, ethyl acetate, butanol, ethanol, methanol, isopropyl alcohol and mixtures thereof.

Claim 101 (original) The method of claim 97 wherein the organic solvent is non-polar.

Claim 102 (original) The method of claim 101 wherein the non-polar organic solvent is dichloromethane or hexane.

Claim 103 (original) The method of claim 97 wherein step (b) further comprises separating the solvent from the organic extract by evaporating the solvent.

Claim 104 (currently amended) A method of treating or preventing COX-2 mediated inflammation or an inflammation-associated disorder in an organism, the method comprising administering to the organism a composition comprising a therapeutically or prophylactically effective amount of the ~~purified composition~~ organic extract according to claim 97.

Claim 105 (original) The method of claim 104 wherein the inflammation-associated disorder is arthritis.

Claims 106-112 (canceled)

Claim 113 (new) The method of claim 97 wherein the inhibitory effect of the extract on COX-2 activity is greater than or equal to about 10 times greater than the inhibitory effect of the extract on COX-1 activity.

Claim 114 (new) The method of claim 1, wherein the organic extract is a crude or partially purified extract.

Claim 115 (new) The method of claim 114, wherein the organic extract is a crude extract.

Claim 116 (new) The method of claim 114, wherein the organic extract is a partially purified extract.

Claim 117 (new) The method of claim 2, wherein the organic extract is a crude or partially purified extract.

Claim 118 (new) The method of claim 117, wherein the organic extract is a crude extract.

Claim 119 (new) The method of claim 117, wherein the organic extract is a partially purified extract.

Claim 120 (new) The method of claim 3, wherein the organic extract is a crude or partially purified extract.

Claim 121 (new) The method of claim 120, wherein the organic extract is a crude extract.

Claim 122 (new) The method of claim 120, wherein the organic extract is a partially purified extract.

Claim 123 (new) The method of claim 60, wherein the organic extract is a crude or partially purified extract.

Claim 124 (new) The method of claim 123, wherein the organic extract is a crude extract.

Claim 125 (new) The method of claim 123, wherein the organic extract is a partially purified extract.

Claim 126 (new) The method of claim 97, wherein the organic extract is a crude or partially purified extract.

Claim 127 (new) The method of claim 126, wherein the organic extract is a crude extract.

Claim 128 (new) The method of claim 126, wherein the organic extract is a partially purified extract.

REMARKS

With this amendment, claims 1-113 are currently pending. Claims 4-57, 59, 61-96, and 106-112 are canceled as being directed to non-elected subject matter. Claims 1, 97, 98, and 104 are currently amended. Claims 113-128 are newly submitted. The amendment to claim 1 is to correct a misspelling. Support for the amendments to claim 97 can be found in the specification at p. 8, lines 7-9 and p. 9, lines 28-34. Support for the amendments to claim 98 can be found in the specification at p. 8, lines 20-22. Support for claim 113 can be found in the specification at p. 8, lines 22-24. Support for claims 114-128 can be found in the specification at p. 6, lines 32-34 and p. 7, lines 1-3.

I. 35 U.S.C. 102(b)

A. LaHann (U.S. Patent No. 4,313,958)

Reconsideration is requested of the rejection of claims 1-3, 58, 60, 97, 98, 100 and 104 under 35 U.S.C. 102(b) as being unpatentable over LaHann (U.S. Patent No. 4,313,958).

As amended, claim 1 is directed to a method of treating an organism for a condition mediated by COX-2 expression by orally, parenterally, or rectally administering to the organism a composition comprising a COX-2 inhibiting amount of an organic extract of *Capsicum frutescens* wherein the extract selectively inhibits the activity of COX-2 relative to COX-1.

LaHann discloses the parenteral and topical administration of capsaicin to treat or prevent pain presumably affiliated with the neurotransmitter substance P.[1]

LaHann does not disclose the administration of an organic extract of *C. frutescens* which selectively inhibits the activity of COX-2 relative to COX-1 in an organism suffering from a condition mediated by COX-2. Instead, LaHann discloses the administration of capsaicin to treat or prevent pain caused by substance P, a pathway distinct from that of the COX-2 pathway. As LaHann does not disclose administration of an extract that selectively inhibits COX-2 to an organism for the treatment of a condition mediated by COX-2, LaHann has failed to disclose each and every element of claim 1.

LaHann also fails to disclose any information from which it can be concluded that capsaicin would ***unavoidably*** selectively inhibit COX-2.[2] *C. frutescens* contains a large number of compositions and it is illogical to conclude that all compositions produced by *C. frutescens* inhibit COX-2. The fact that applicants have successfully prepared an extract from *C. frutescens* which inhibits COX-2, therefore, does not support a

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[1] *See*, LaHann, U.S. Patent No. 4,313,958, col. 2, lines 32-41, wherein LaHann incorporates by reference Virus, R.M. & Geonart, G.F., "Miniriview - The Pharmacologic Actions of Capsaicin: Apparent Involvement of Substance P and Serotonin," *Life Sciences*, 25, 1273 (1979); *see also*, Byas-Smith, U.S. Patent No. 5,762,963, col 3., line 55 through col. 4, line 9.

[2] Inherency can be found only where attainment of a claimed feature is unavoidable, not where it is merely possible or even probable. *Continental Can v. Monsanto*, 20 USPQ2d 1746 (Fed. Cir. 1991); *ex parte Keith*, 154 USPQ 320 (PTO Bd App 1966); *in re Oelrich*, 212 USPQ 323 (CCPA 1981); *In re Rijckaert*, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993).

conclusion that capsaicin, when isolated from *C. frutescens*, selectively inhibits COX-2. In the absence of any evidence as described by LaHann or rationale to the contrary, the Office has failed to establish a *prima facie* determination of inherency.[3]

Claims 2, 3, 58, 60, 97, 98, 100, 104, 105, and 113-128 depend from claim 1 and are patentable over LaHann for the reasons stated with respect to claim 1 and by reason of the additional requirements which they introduce.

B. GB 2,168,975 (Janusz et al.)

Reconsideration is requested of the rejection of claims 1-3, 58, 60, 97, 98, 100 and 104 under 35 U.S.C. 102(b) as being unpatentable over GB 2,168,975 ("GB '975").

As stated in greater detail above in Section I.A., claim 1, as amended, is directed to a method of treating an organism for a condition mediated by COX-2 expression.

GB '975 discloses that "certain araalkanamides have anti-inflammatory and analgesic activity similar to that of non-steroidal analgesics such as aspirin in human and lower animals,"[4] and that "**[t]hese araalkanamides are far less toxic than capsaicin.**"[5] GB '975 also discloses "that capsaicin, a natural product of certain species of the genus *Capsicum*, induces analgesia."[6] GB '975 further discloses a list of various

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[3] To properly support a determination of inherency, as a matter of Patent Office practice, it is incumbent on the Examiner to provide rationale or evidence. See MPEP § 2112.

[4] GB 2 168 975, p. 1, lines 52-53

[5] GB 2 168 975, p. 1, lines 53-54 (emphasis added).

[6] GB 2 168 975, p. 1, lines 34-35.

references that are asserted to disclose the analgesic and anti-irritant activity of capsaicin, including LaHann.[7]

Araalkanamides and capsaicin are not the same, as demonstrated by the disclosure in GB '975 that araalkanamides are far less toxic than capsaicin. In addition, these araalkanamides are not obtained by the extraction of *C. frutescens*, but are instead synthesized and said to also be commercially available. Therefore, regardless of any use or any route of administration that may be disclosed therein, the disclosure of the use of araalkanamides as anti-inflammatory and analgesic agents does not anticipate claim 1.

Accordingly, GB '975 fails to disclose each and every element of claim 1, and therefore does not anticipate claim 1.

Claims 2, 3, 58, 60, 97, 98, 100, 104, 105, and 113-128 depend from claim 1 and are patentable over GB '975 for the reasons stated with respect to claim 1 and by reason of the additional requirements which they introduce.

C. Byas-Smith (U.S. Patent No. 5,762,963)

Reconsideration is requested of the rejection of claims 1-3, 58, 60, 97, 98, 100, 104, and 105 under 35 U.S.C. 102(b) as being unpatentable over Byas-Smith (U.S. Patent No. 5,762,963).

As stated in greater detail above in Section I.A., claim 1, as amended, is directed to a method of treating an organism for a condition mediated by COX-2 expression.

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[7] GB 2 168 975, p. 1, lines 34-51. *See also*, p. 1, lines 35-36 ("Capsaicin (8-methy-N-vanillyl-6-nonenamide) and 'synthetic' capsaicin (N-vanillylnonamide) are disclosed as analgesics in U.S. Patent 4,313,958, LaHann, issued February 2, 1982.").

Byas-Smith discloses methods and compositions for the oral delivery of an increasing amount of capsaicin, capsaicin derivatives, or capsaicin analogs, and one or more capsaicinoids, for the relief of oral and pharyngeal pain while minimizing side effects such as nausea and burning typically associated with the oral administration of capsaicinoids. It is further disclosed that indications that may be treated by the disclosed methods and compositions include all inflammatory pain and neuropathic pain conditions involving the oral cavity, oral pharynx, and other painful mucosal pathology along the course of the gastrointestinal tract.

Byas-Smith does not disclose the administration of an organic extract of *C. frutescens* which selectively inhibits the activity of COX-2 relative to COX-1 in an organism suffering from a condition mediated by COX-2. Instead, Byas-Smith discloses the administration of capsaicin to treat or prevent pain caused by substance P, a pathway distinct from that of the COX-2 pathway. As Byas-Smith does not disclose administration of an extract that selectively inhibits COX-2 to an organism for the treatment of a condition mediated by COX-2, Byas-Smith has failed to disclose each and every element of claim 1.

Moreover, Byas-Smith does not disclose an ethanol extract of capsaicin administered orally to treat arthritis (a COX-2 mediated condition) as asserted by the Office. A search of the reference demonstrates that the only use of the word "arthritis" occurs with respect to the use of the **topical** prescription drugs Zostrix®, Zostrix-HP®, and Axsain® to treat rheumatoid arthritis and osteoarthritis.[8] There is no other disclosure of the word

[8] Byas-Smith, U.S. Patent No. 5,762,963, column 4, lines 19-27.

arthritis nor any indication of the treatment of arthritis other than by topical application of the aforementioned drugs. Accordingly, there is no disclosure of the oral administration of an ethanol extract of capsaicin to treat arthritis.

In addition, as discussed above with respect to LaHann, *C. frutescens* contains a large number of compositions and it is illogical to conclude that all compositions produced by *C. frutescens* inhibit COX-2. The fact that applicants have successfully prepared an extract from *C. frutescens* which inhibits COX-2, therefore, does not support a conclusion that capsaicin, when isolated from *C. frutescens*, selectively inhibits COX-2. In the absence of any evidence as described by Byas-Smith or rationale to the contrary, the Office has failed to establish a *prima facie* determination of inherency.[9]

Claims 2, 3, 58, 60, 97, 98, 100, 104, 105, and 113-128 depend from claim 1 and are patentable over Byas-Smith for the reasons stated with respect to claim 1 and by reason of the additional requirements which they introduce.

II. 35 U.S.C. 102(e)

Reconsideration is requested of the rejection of claims 1-3, 58, 60, 97, 98, 100, 104, and 105 under 35 U.S.C. 102(e) as being unpatentable over De Lucca, II et al. (U.S. Patent No. 6,310,091).

As stated in greater detail above in Section I.A., claim 1, as amended, is directed to a method of treating an organism for a condition mediated by COX-2 expression.

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[9] To properly support a determination of inherency, as a matter of Patent Office practice, it is incumbent on the Examiner to provide rationale or evidence. See MPEP § 2112.

De Lucca, II et al. disclose an antifungal compound isolated from *C. frutescens*, designated CAY-1. CAY-1 is obtained by the extraction of *C. frutescens* with a suitable solvent, followed by separation of the solid and liquid fraction, elution of the liquid fraction with methanol, and then further purification to homogeneity from the methanol eluate such as by liquid chromatography, high performance liquid chromatography, or the like, resulting in a **single compound purified to homogeneity.** CAY-1 is disclosed to have **only** antifungal properties and can be administered to animals through various routes, including orally, rectally, and parenterally.

Significantly, and similar to Byas-Smith, the only disclosure in De Lucca, II et al. of the use of capsaicin to treat a COX-2 mediated condition, in this case arthritis, is a reference in the Background of the Invention to the **topical** creams Zostrix® and Axsain®. There is no disclosure to indicate that capsaicin-based compositions can be administered by means other than topically to treat a COX-2 mediated disorder such as arthritis. Accordingly, De Lucca, II et al, have failed to disclose each and every element of claim 1.

Moreover, the only disclosure of an oral, rectal, or parenteral administration of a compound in De Lucca, II et al. is the administration of the purified compound CAY-1 for use as an antifungal. De Lucca, II et al. disclose that the isolation of CAY-1 required extraction of *C. frutescens*, followed by the additional steps of separation of the liquid and solid phases, elution of the liquid phase, and further purification techniques such as liquid chromatography, high performance liquid

chromatography, or the like.[10] Moreover, De Lucca, II et al. disclose that CAY-1 is one of but a few compounds that have been isolated from this particular pepper family.[11] Therefore, even assuming *arguendo* that the initial extract of De Lucca, II et al. would demonstrate COX-2 inhibiting activity, it cannot be said that the CAY-1 compound purified therefrom would ***unavoidably*** retain such COX-2 inhibiting activity, as it is illogical to conclude that all compositions produced by *C. frutescens* inhibit COX-2. The fact that applicants have successfully prepared an extract from *C. frutescens* which inhibits COX-2, therefore, does not support a conclusion that CAY-1, when isolated from *C. frutescens*, selectively inhibits COX-2. In the absence of any evidence as described by De Lucca, II et al. or rationale to the contrary, the Office has failed to establish a *prima facie* determination of inherency.[12]

Claims 2, 3, 58, 60, 97, 98, 100, 104, 105, and 113-128 depend from claim 1 and are patentable over De Lucca, II et al. for the reasons stated with respect to claim 1 and by reason of the additional requirements which they introduce.

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[10] De Lucca, II et al., at Column 5, lines 10-31; *See also*, Example 1 at Column 7, line 30 through Column 8, line 2.

[11] De Lucca, II et al. at Column 3, line 53, and Column 4, line 28.

[12] To properly support a determination of inherency, as a matter of Patent Office practice, it is incumbent on the Examiner to provide rationale or evidence. See MPEP § 2112.

III. 35 U.S.C. 103(a)

A. De Lucca, II et al. or Byas-Smith taken with Hawley's Condensed Chemical Dictionary

Reconsideration is requested of the rejection of claims 1-3, 58, 60, and 97-105 under 35 U.S.C. 103(a) as being unpatentable over De Lucca, II et al. or Byas-Smith taken with Hawley's Condensed Chemical Dictionary ("Hawley's").

As stated in greater detail above in Section I.A., claim 1, as amended, is directed to a method of treating an organism for a condition mediated by COX-2 expression.

De Lucca, II et al. disclose the use of a compound isolated and **purified** from *C. frutescens*, designated CAY-1, as an antifungal and further disclose the existence of **topical** creams based upon capsaicin for the treatment of pain related to arthritis.

Byas-Smith suggests the relief of oral or pharyngeal pain by the administration of an increasing amount of capsaicin, a **purified** compound, resulting in the depletion of Substance P from local sensory terminals, and, similar to De Lucca, II et al., further discloses the existence of **topical** creams based upon capsaicin for the treatment of the pain associated with arthritis.

Hawley's merely discloses that methylene chloride (dichloromethane) can be used for solvent extraction.

The Office has failed to establish a *prima facie* case of obviousness, as the references, when combined, fail to teach or suggest each and every limitation of claim 1.[13] Specifically, each of these references fails to teach or suggest an organic

[13] MPEP §2142.

extract of *C. frutescens* that inhibits COX-2 and the oral, parenteral, or rectal administration of such an extract in a COX-2 inhibiting amount in order to selectively inhibit COX-2 in an organism suffering from a condition mediated by COX-2 expression. As each individual reference fails to teach each of these elements, it cannot be asserted that the combination of the five cures this deficiency. Therefore, because the combination of references fails to teach or suggest all such claim limitations, the Office has failed to establish a *prima facie* case of obviousness.[14]

In addition, the Office has failed to establish a *prima facie* case of obviousness as there is no motivation or suggestion within the references themselves or in the knowledge generally available to one of skill in the art to modify or combine the reference teachings.[15] De Lucca, II et al. and Byas-Smith disclose the administration of two different **purified** compounds. Hawley's, merely discloses the fact that methylene chloride can be used as an extraction solvent. There is nothing contained within these references that would motivate one of skill in the art to simply prepare an organic extract of *C. frutescens*, foregoing subsequent purification of the same into one of the purified compounds disclosed in De Lucca, II et al. or Byas-Smith, and to orally, parenterally, or rectally administer such a composition comprising a COX-2 inhibiting organic extract of *C. frutescens* to an organism suffering from a condition mediated by COX-2.

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[14] MPEP §2142.

[15] MPEP §2142.

Accordingly, there is no motivation or suggestion within the references themselves or in the knowledge generally available to one of skill in the art to combine or modify these three references to achieve the invention of claim 1, and therefore, the Office has failed to establish a *prima facie* case of obviousness.[16]

Claims 2, 3, 58, 60, 97-105 and 113-128 depend from claim 1 and are patentable over De Lucca, II et al. or Byas-Smith taken with Hawley's for the reasons stated with respect to claim 1 and by reason of the additional requirements which they introduce.

B. De Lucca, II et al. or Byas-Smith taken with LaHann or GB '975 and Hawley's

Reconsideration is requested of the rejection of claims 1-3, 58, 60, and 97-105 under 35 U.S.C. 103(a) as being unpatentable over De Lucca, II et al. or Byas-Smith taken with LaHann or GB '975 and Hawley's.

As stated in greater detail above in Section I.A., Claim 1, as amended, is directed to a method of treating an organism for a condition mediated by COX-2 expression.

De Lucca, II et al., Byas-Smith, and Hawley's are discussed above in Section III A., and do not render the claimed invention obvious for the reasons stated therein.

LaHann discloses the parenteral administration of the **purified** compound capsaicin to treat or prevent pain presumably affiliated with the neurotransmitter substance P.[17]

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[16] MPEP §2142.

[17] *See*, footnote 1 above.

GB '975 discloses the administration of araalkanamides as analgesic and anti-inflammatory agents. It further discloses a list of various references, including LaHann, that are asserted to disclose the analgesic and anti-irritant activity of capsaicin.

Even when combined, these references fail to teach or suggest all limitations of claim 1. De Lucca, II et al., LaHann, and Byas-Smith disclose the administration of a **purified** compound for use as an antifungal or analgesic, and not the administration of a COX-2 inhibiting organic extract of *C. frutescens* for the treatment of COX-2 mediated disorders. The '975 application, aside from its cursory reference to LaHann and similar articles, discloses the use of a group of unrelated compounds for the treatment of pain and inflammation. Therefore, even when combined, the references fail to teach or suggest an organic extract of *C. frutescens* which inhibits COX-2, and the oral, parenteral, or rectal administration of such an extract in a COX-2 inhibiting amount in order to selectively inhibit COX-2 in an organism suffering from a condition mediated by COX-2 expression. Because the combination of references fails to teach or suggest all such claim limitations, the Office has failed to establish a *prima facie* case of obviousness.[18]

In addition, the Office has failed to establish a *prima facie* case of obviousness as there is no motivation or suggestion within the references themselves or in the knowledge generally available to one of skill in the art to modify or combine the reference teachings.[19] As discussed above in Section III.A.,

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[18] MPEP §2142.

[19] MPEP §2142.

there is no motivation or suggestion to combine or modify De Lucca, II et al., Byas-Smith, and Hawley's. Moreover, this lack of motivation or suggestion to combine is not cured by LaHann or GB '975.

LaHann, like De Lucca, II et al. and Byas-Smith, would not motivate one of skill in the art to simply prepare an organic extract of *C. frutescens*, foregoing the subsequent purification of the same into one of the purified compounds disclosed therein. GB '975, does nothing to cure this lack of motivation, as it merely discloses the administration of various synthetically prepared araalkanamides as anti-inflammatory and analgesic agents. Nothing in the combination of references would motivate one of skill in the art to prepare an organic extract of *C. frutescens* for selectively inhibiting COX-2 and to use such an extract to treat an organism suffering from a condition mediated by COX-2.

Accordingly, there is no motivation or suggestion within the references themselves or in the knowledge generally available to one of skill in the art to combine or modify these three references to achieve the invention of claim 1, and therefore, the Office has failed to establish a *prima facie* case of obviousness.[20]

Claims 2, 3, 58, 60, 97-105, and 113-128 depend from claim 1 and are patentable over De Lucca, II et al. or Byas-Smith taken with LaHann or GB '975 and Hawley's for the reasons stated with respect to claim 1 and by reason of the additional requirements which they introduce.

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[20] MPEP §2142.

C. Holt et al., Stevens, Barr et al., or Caruso in view of LaHann or GB '975 taken with Hawley's.

Reconsideration is requested of the rejection of claims 1-3, 58, 60, and 97-105 under 35 U.S.C. 103(a) as being unpatentable over Holt et al. (U.S. Patent No. 6,348,501), Stevens (U.S. Patent No. 4,324,785), Barr et al. (U.S. Patent No. 6,197,823), or Caruso (U.S. Patent No. 6,277,398) in view of LaHann or GB '975 taken with Hawley's.

As stated in greater detail above in Section I.A., claim 1 is directed to a method of treating an organism for a condition mediated by COX-2 expression.

Holt et al. disclose a **topical lotion** for treating the symptoms of arthritis containing the **purified compound capsaicin**, an anesthetic, and an analgesic. The lotion is used to treat the pain associated with arthritis. Holt et al. do not disclose the oral, rectal, or parenteral administration of a COX-2 inhibiting organic extract of *C. frutescens*.

Stevens discloses a powder for use on feet exposed to the cold to provide a feeling of warmth comprising different amounts and combinations of powdered cayenne pepper, powdered ginger, powdered mustard, and at least one powdered aromatic substance. In the Background of the Invention, Stevens discloses that heat producing preparations providing a sense of warmth to painful areas of the body are well known, including preparations comprising capsicum oleoresin, for the treatment of muscle pain and arthritis. Stevens does not disclose the oral, rectal, or parenteral administration an organic extract of *C. frutescens*.

Barr et al. disclose **topical** creams, ointments, foams, and the like, that contain capsaicin and that can be used to treat pain and discomfort associated with disorders such as arthritis.

Barr et al. do not disclose the oral, rectal, or parenteral administration of an organic extract of *C. frutescens*.

Caruso discloses an analgesic drug composition containing a capsaicinoid, such as capsaicin, as an analgesic component, and dextromethorphan, its active metabolite, dextrorphan, and/or a pharmaceutically acceptable salt thereof, as a potentiator for the capsaicinoid, thereby enhancing its analgesic effect. Caruso discloses that the analgesic drug composition can be formulated for oral, topical, parenteral, etc. administration. However, the only example of such a drug composition is the use of capsaicin in a non-occlusive adhesive patch. Moreover, the only disclosure of the use of an extract of capsicum is the passing mention of the use of capsicum oleoresin in well-known over the counter **topical** analgesic medications. Caruso does not disclose the oral, rectal, or parenteral administration of an organic extract of *C. frutescens*.

LaHann, GB '975, and Hawley's are discussed above in Section III B., and do not render the claimed invention obvious for the reasons stated therein.

Even when combined, these references fail to teach or suggest all limitations of claim 1. There is nothing contained within the references, either singly or in combination, that teaches or suggests an organic extract of *C. frutescens* which inhibits COX-2, and the oral, parenteral, or rectal administration of such an extract in a COX-2 inhibiting amount in order to selectively inhibit COX-2 in an organism suffering from a condition mediated by COX-2 expression. Because the combination of references fails to teach or suggest all such

claim limitations, the Office has failed to establish a *prima facie* case of obviousness.[21]

In addition, the Office has failed to establish a *prima facie* case of obviousness as there is no motivation or suggestion within the references themselves or in the knowledge generally available to one of skill in the art to modify or combine the reference teachings.[22] As discussed above in Section III.B., there is no motivation or suggestion to combine or modify LaHann, GB '975, and Hawley's. Moreover, this lack of motivation or suggestion to combine is not cured by Holt et al., Stevens, Barr et al., or Caruso. Holt et al., Stevens, and Barr et al. merely disclose topical compositions. Caruso, although passingly mentioning that the composition disclosed therein could be formulated for oral, parenteral, or topical administration, only discloses examples of topical administration of the compound, with respect not only to the sole demonstrated embodiment of the invention, but also with respect to well-known prior art medications. Nothing in the references would motivate one of skill in the art to prepare an organic extract of *C. frutescens* for selectively inhibiting COX-2, and to use such an extract for oral, parenteral, or rectal administration to an organism suffering from a condition mediated by COX-2 to treat the same by selectively inhibiting COX-2. In fact, if anything, Holt et al., Stevens, Barr et al., and Caruso would lead one of skill to believe that compositions containing capsaicin should only be administered topically, and therefore, these references teach away from the presently claimed invention.

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[21] MPEP §2142.

[22] MPEP §2142.

Accordingly, there is no motivation or suggestion within the references themselves or in the knowledge generally available to one of skill in the art to combine or modify these three references to achieve the invention of claim 1, and therefore, the Office has failed to establish a *prima facie* case of obviousness.[23]

Claims 2, 3, 58, 60, 97-105 and 113-128 depend from claim 1 and are patentable over Holt et al., Stevens, Barr et al., or Caruso in view of LaHann or GB '975 taken with Hawley's for the reasons stated with respect to claim 1 and by reason of the additional requirements which they introduce.

D. LaHann or GB '975 taken with Hawley's

Reconsideration is requested of the rejection of claims 1-3, 58, 60, and 97-105 under 35 U.S.C. 103(a) as being unpatentable over LaHann or GB '975 taken with Hawley's.

As stated in greater detail above in Section I.A., claim 1 is directed to a method of treating an organism for a condition mediated by COX-2 expression.

LaHann discloses the parenteral administration of the purified compound capsaicin to treat or prevent pain. It does not disclose the administration of a COX-2 inhibiting organic extract of *C. frutescens*.

GB '975 discloses the administration of araalkanamides as analgesic and anti-inflammatory agents. It further discloses a list of various references, including LaHann, that are asserted to disclose the analgesic and anti-irritant activity of the purified compound capsaicin. GB '975 does not disclose the oral,

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[23] MPEP §2142.

rectal, or parental administration of COX-2 inhibiting organic extract of *C. frutescens*.

Hawley's merely demonstrates that methylene chloride (dichloromethane) can be used for solvent extraction.

Even when combined, these references fail to teach or suggest all limitations of claim 1. There is nothing contained within the references, either singly or in combination, that teaches or suggests an organic extract of *C. frutescens* which inhibits COX-2, and the oral, parenteral, or rectal administration of such an extract in a COX-2 inhibiting amount in order to selectively inhibit COX-2 in an organism suffering from a condition mediated by COX-2 expression. Because the combination of references fails to teach or suggest all such claim limitations, the Office has failed to establish a *prima facie* case of obviousness.[24]

In addition, the Office has failed to establish a *prima facie* case of obviousness as there is no motivation or suggestion within the references themselves or in the knowledge generally available to one of skill in the art to modify or combine the reference teachings.[25] As discussed above in Section III.B., there is no motivation or suggestion to combine or modify LaHann, GB '975, and Hawley's.

Accordingly, there is no motivation or suggestion within the references themselves or in the knowledge generally available to one of skill in the art to combine or modify these references to

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[24] MPEP §2142.

[25] MPEP §2142.

achieve the invention of claim 1, and therefore, the Office has failed to establish a *prima facie* case of obviousness.[26]

Claims 2, 3, 58, 60, 97-105, and 113-128 depend from claim 1 and are patentable over LaHann or GB '975 taken with Hawley's for the reasons stated with respect to claim 1 and by reason of the additional requirements which they introduce.

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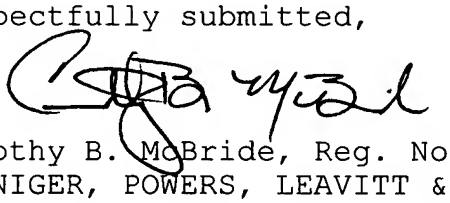
[26] MPEP §2142.

CONCLUSION

In light of the above arguments, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-3, 58, 60, 97, 98, 100, 104, and 105 under 35 U.S.C. 102(b) and 102(e) and of claims 1-3, 58, 60, and 97-105 under 35 U.S.C. 103(a).

Applicants request an extension of time to and including October 18, 2003, for filing a response to the above-mentioned Office action. A check in the amount of the applicable extension fee is enclosed. The Commissioner is hereby authorized to charge any deficiency or overpayment in connection with this amendment to Deposit Account No. 19-1345.

Respectfully submitted,



Timothy B. McBride, Reg. No. 47,781
SENNIGER, POWERS, LEAVITT & ROEDEL
One Metropolitan Square, 16th Floor
St. Louis, Missouri 63102
(314) 231-5400

TBM/sxm/msc
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